

## Improved Alphavirus Vectors Having Attenuated Virion Structural Proteins

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### Abstract

The present invention provides immunogenic compositions and methods that may be used to administer safer (*i.e.*, attenuated) alphavirus vectors (such as alphavirus vectors comprising a VEE virion shell) that retain improved immunogenicity as compared with other attenuated alphaviruses (e.g., the VEE 3014 mutant, described below). In particular embodiments of the invention, the alphavirus vector comprises VEE structural proteins comprising an attenuating mutation in the E1 glycoprotein. In other particular embodiments, the attenuating mutation is in the fusogenic region of the E1 glycoprotein. The present invention enables administration of lower dosages of a safer (*i.e.*, attenuated) virus and, thus, can further reduce manufacturing costs. The present inventors have found that immunogenicity of alphavirus vectors may be influenced by a number of factors including species, site and route of administration.

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